

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:        **ISPH-0795**

Inventors:                    **Ackermann et al.**

Serial No.:                   **Not Yet Assigned**

Filing Date:                 **Herewith**

Examiner:                    **Not Yet Assigned**

Group Art Unit:              **Not Yet Assigned**

Title:                         **Antisense Modulation of FLIP-c  
Expression**

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By *Jane Massey Licata*  
Typed Name: **Jane Massey Licata, Reg. No. 32,257**

Mail Stop Sequence  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA    22313-1450

Sir:

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

(XX) In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, no additional fee is required.

( ) In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, therefore:

( ) Certification in Accordance with §1.97(e) is set forth below; or

( ) The fee of \$180.00 as set forth in §1.17(p) is attached.

( ) In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); Petition Requesting Consideration of the Information Disclosure Statement; and the fee of \$130.00 as set forth in §1.17(I)(1).

( ) Copies of each of the references listed on the attached Form PTO-1449 (modified) are enclosed herewith.

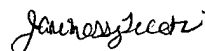
(XX) In accordance with §1.98(d), copies of some or all of the references listed on the attached Form PTO-1449 (modified) are not enclosed herewith because they were previously submitted to the U.S. Patent and Trademark Office in prior application Serial No. 09/666,269, filed September 20, 2000, for which a claim for priority under 35 U.S.C. §120 has been made in the instant application.

Please charge any deficiency or credit any overpayment to Deposit Account No. 50-1619. This form is submitted in duplicate.

( ) The relevance of the listed references in a foreign language is as stated in the specification at pages @@.

(XX) All listed references are in the English language.

Respectfully submitted,



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Date: October 27, 2003

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Form PTO-1449 Modified		Docket No. <b>ISPH-0795</b>	Serial No. not yet assigned
List of Patents and Publications Cited by Application (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Applicant Elizabeth J. Ackermann et al.	
		Filing Date herewith	Group
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AA	Bantel et al., Mistletoe lectin activates caspase-8/FLICE independently of death receptor signaling and enhances anticancer drug-induced apoptosis, Cancer - Res., 1999, 59:2083-2090	
	AB	Bartz et al., Human immunodeficiency virus type 1 Tat induces apoptosis and increases sensitivity to apoptotic signals by up-regulating FLICE/caspase-8, J. Virol., 1999, 73:1956-1963	
	AC	Bitzer et al., Sendai Virus Infection Induces Apoptosis through Activation of Caspase- 8 (FLICE) and Caspase-3 (CPP32), J. Virol., 1999, 73:702-708	
	AD	Chlichlia et al., Caspase activation is required for nitric oxide-mediated, CD95(APO- 1/Fas)-dependent and independent apoptosis in human neoplastic lymphoid cells, Blood, 1998, 91:4311-4320	
	AE	Coltsev et al., CASH, a novel caspase homologue with death effector domains, J. Biol. Chem., 1997, 272:19641-19644	
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	AG	Hu et al., I-FLICE, a novel inhibitor of tumor necrosis factor receptor-1- and CD- 95-induced apoptosis, J. Biol. Chem., 1997, 272:17255-17257	
	AH	Imanishi et al., Expression of cellular FLICE-inhibitory protein in human coronary arteries and in a rat vascular injury model, Am. J. Pathol., 2000, 156:125-137	
	AI	Inohara et al., CLARP, a death effector domain-containing protein interacts with caspase-8 and regulates apoptosis, Proc. Natl. Acad. Sci. U. S. A., 1997, 94:10717-10722	
	AJ	Irmeler et al., Inhibition of death receptor signals by cellular FLIP, Nature, 1997, 388:190-195	
	AK	Konopleva et al., Apoptosis. Molecules and mechanisms, Adv. Exp. Med. Biol., 1999, 457:217-236	
EXAMINER		DATE CONSIDERED	

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AL	Kuwana et al., <del>Apoptosis induction by caspase-8 is amplified through the mitochondrial release of cytochrome c</del> , J. Biol. Chem., 1998, 273:16589-16594	
	AM	Leverkus et al., Regulation of tumor necrosis factor-related apoptosis-inducing ligand sensitivity in primary and transformed human keratinocytes, Cancer Res., 2000, 60:553-559	
	AN	Luschen et al., Cleavage of human cytosolic phospholipase A2 by caspase-1 (ICE) and caspase-8 (FLICE), Biochem. Biophys. Res. Commun., 1998, 253:92-98	
	AO	Mandruzzato et al., A CASP-8 mutation recognized by cytolytic T lymphocytes on a human head and neck carcinoma, J. Exp. Med., 1997, 186:785-793	
	AP	Martin et al., Membrane oligomerization and cleavage activates the caspase-8 (FLICE/MACHalpha1) death signal, J. Biol. Chem., 1998, 273:4345-4349	
	AQ	Medema et al., FLICE is activated by association with the CD95 death-inducing signaling complex (DISC), Embo J., 1997, 16:2794-2804	
	AR	Medema et al., Cleavage of FLICE (caspase-8) by granzyme B during cytotoxic T lymphocyte-induced apoptosis, Eur. J. Immunol., 1997, 27:3492-3498	
	AS	Muzio et al., FLICE, a novel FADD-homologous ICE/CED-3-like protease, is recruited to the CD95 (Fas/APO-1) death-inducing signaling complex, Cell, 1996, 85:817-827	
	AT	Muzio et al., An induced proximity model for caspase-8 activation, J. Biol. Chem., 1998, 273:2926-2930	
	AU	Perlman et al., FLICE-inhibitory protein expression during macrophage differentiation confers resistance to fas-mediated apoptosis, J. Exp. Med., 1999, 190:1679-1688	
	AV	Peter et al., AIDS and the death receptors, Br. Med. Bull., 1997, 53:604-616	

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	AW	Que et al., Cholangiocarcinomas express Fas ligand and disable the Fas receptor, Hepatology, 1999, 30:1398-1404	
	AX	Rasper et al., Cell death attenuation by 'Usurpin', a mammalian DED-caspase homologue that precludes caspase-8 recruitment and activation by the CD-95 (Fas, APO-1) receptor complex, Cell Death Differ., 1998, 5:271-288	
	AY	Scaffidi et al., The role of c-FLIP in modulation of CD95-induced apoptosis, J. Biol. Chem., 1999, 274:1541-1548	
	AZ	Shu et al., Casper is a FADD- and caspase-related inducer of apoptosis, Immunity, 1997, 6:751-763	
	BA	Srinivasula et al., Molecular ordering of the Fas-apoptotic pathway: the Fas/APO-1 protease Mch5 is a CrmA-inhibitable protease that activates multiple Ced-3/ICE- like cysteine proteases, Proc. Natl. Acad. Sci. U. S. A., 1996, 93:14486-14491	
	BB	Srinivasula et al., FLAME-1, a novel FADD-like anti-apoptotic molecule that regulates Fas/TNFR1-induced apoptosis, J. Biol. Chem., 1997, 272:18542-18545	
	BC	Tepper et al., Modulation of caspase-8 and FLICE-inhibitory protein expression as a potential mechanism of Epstein-Barr virus tumorigenesis in Burkitt's lymphoma, Blood, 1999, 94:1727-1737	
	BD	Thornberry, The caspase family of cysteine proteases, Br. Med. Bull., 1997, 53:478-490	
	BE	Tschopp et al., Inhibition of fas death signals by FLIPs, Curr. Opin. Immunol., 1998, 10:552-558	
	BF	Wang et al., Inhibition of Fas-mediated apoptosis by the B cell antigen receptor through c-FLIP, Eur. J. Immunol., 2000, 30:155-163	
	BG	Wesselborg et al., Anticancer drugs induce caspase-8/FLICE activation and apoptosis in the absence of CD95 receptor/ligand interaction, Blood, 1999, 93:3053-3063	
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U.S. Department of Commerce Patent and Trademark Office	Filing Date	Group

**U.S. PATENT DOCUMENTS**

Examiner's Initial		Document No.	Date	Name	Class	Subclass
	AA	6,037,461	03/14/2000	Alnemri	536	23.5
	AB					
	AC					
	AD					
	AE					
	AF					
	AG					
	AH					
	AI					
	AJ					
	AK					
	AL					
	AM					
	AN					

**FOREIGN PATENT DOCUMENTS**

Examiner's Initial		Document No.	Date	Country	Translation YES NO	
	AO	WO 98/52963	11/26/1998	PCT		
	AP	WO 98/44103	10/08/1998	PCT		X
	AQ	WO 00/03023	01/20/2000	PCT		
	AR	WO '99/42570	08/26/1999	PCT		
	AS					
	AT					
	AU					
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	AX					

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